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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
07/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-63* is/are pending in the application.

4a) Of the above claim(s) *39,40,61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-38,41-60 and 63* is/are rejected.

7)☒ Claim(s) *41-60* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/26/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. New claims 61-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/20/2007.

Response to Arguments

2. Applicants' arguments, filed 3/26/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

3. Applicant's arguments, see pp. 11-14, filed 3/26/2008, with respect to the rejections of claims 19-24 and 31, of claim 19 and of claims 19-38 under 35 USC 102 have been fully considered and are persuasive. The rejections of claims 19-24 and 31, 19 and 19-38 have been withdrawn.

Applicant's arguments that neither Gamache nor Dobrozsi concretely describe the combination of bromfenac and tyloxapol, recited in the amended claims, are persuasive. Therefore the rejections based on Gamache and Dobrozsi are withdrawn. Applicant's argument that Sawa does not have a proper 102(e) date is also persuasive.

4. Applicant's arguments, see pp. 15-17, filed 3/26/2008, with respect to rejection of claims 19-29, 31-34 and 36-38 under 35 USC 103 have been fully considered and are persuasive. The rejection of claims 19-29, 31-34 and 36-38 has been withdrawn.

Applicant's arguments that neither Gamache nor Dobrozsi concretely describe the combination of bromfenac and tyloxapol, recited in the amended claims, are persuasive. Therefore the rejections based on Gamache and Dobrozsi are withdrawn. Applicant's arguments that Sawa does not have a 102(e) date is persuasive.

5. Applicant's arguments with respect to the rejection of claims 19-29, 31-34 and 36-38 as being unpatentable over Gamache and ISTA Pharmaceuticals or Nolan have been fully considered but they are not persuasive:

6. Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001; previously cited) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007; previously cited) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenic in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; provided with Interview Summary).

The rejection is maintained for the reasons of record and the following reasons.

Applicant argues that Gamache does not suggest the claimed invention, because Gamache is directed to 5-HT agonists compositions with a great number of other possible ingredients; the reference does not suggest the required combination of bromfenac and tyloxapol. This is not persuasive. Gamache clearly teaches combinations of 5-$HT_{1B/1D}$ agonists with one or more anti-inflammatory agents, dosed concurrently or sequentially with anti-inflammatory agent compositions. (p. 12, lines 9-11); bromfenac is clearly taught as an anti-inflammatory compound specie (p. 12, line

17; claim 11). This implies two different compositions as embodiments: 1) a composition containing a 1B/1D agonist and an anti-inflammatory agent (such as in claims 7, 10-11) and 2) two different compositions, where the first contains only an anti-inflammatory agent as the active compound, the second contains only a 1B/1D agonist as active agent (implied by sequential dosing). Taking Example 4 as the model formulation, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute bromfenac for Moxifloxin taught in the example, giving an aqueous liquid preparation containing both required ingredients of the instant claims, bromfenac and tyloxapol (along with the 5-$HT_{1B/1D}$ agonists). Alternatively, it would have been obvious to substitute bromfenac for both Moxifloxin and the 1B/1D agonist, giving an aqueous liquid preparation containing both required ingredients of the instant claims, bromfenac and tyloxapol (without a 5-$HT_{1B/1D}$ agonist). The motivation to prepare the combination formulation (with two active ingredients) would have been for the treatment of otic inflammatory reactions and responses, taught by Gamache (on p. 12, lines 8-11). The motivation to prepare the single active formulation (without a 5-$HT_{1B/1D}$ agonist) would have been for the sequential treatment of otic inflammatory reactions and responses, taught by Gamache. The motivation to select bromfenac as the anti-inflammatory agent would have been the art-recognized usefulness for the purpose of treating inflammatory reactions and responses, recognized by Gamache, and bomfenac sodium at the concentrations of the claims is taught by ISTA Pharmaceuticals and Nolan, also suitable for the purpose of Gamache's formulations. With respect to the tyloxapol concentrations recited in instant claims 25 and 32, of “about 0.02 w/v%” and

"about 0.3 w/v%", the amount taught is considered to be close, if not within the unspecified range implied by "about". Alternatively, it would have been obvious to optimize concentrations of tyloxapol, which one of ordinary skill in the art would have recognized is a surfactant, to optimize the conditions of the formulations for solubility of other ingredients, stability and efficacy in the anti-inflammatory action of the formulation, which would have given tyloxapol concentrations of the instant claims. The motivation would have been the routine optimization of conditions.

Applicant argues that ISTA Pharmaceuticals press release about Xibrom has a different composition than the instant formulation. This point is not at issue; the reference was cited to demonstrate salts and hydrates of bromfenac and concentrations of the instant claims. Applicant also argues the ISTA reference of the Nolan reference in combination with Gamache does not suggest the claimed invention comprising the at least two components. This is not persuasive because Gamache alone suggests the combination of the two required components, as outlined above.

Applicant argues that the combination of a 1B/1D agonist with bromfenac would not read on claims 41-60 because of the recitation of the "consisting essentially of" transitional phrase. This is not persuasive, since the phrase "at least" after "consisting essentially of" in claim 41 opens the subject matter to any additional ingredients. Even if the "at least" were absent from the claim language, the embodiment suggested by Gamache of only one single active anti-inflammatory agent (useful in a sequential treatment method) would obviate such a claim construction. With respect to claim 63, even if the "comprising" language was replaced by "consisting of" language, the

substitution of bromfenac for the active ingredients in Example 4 as suggested by Gamache would produce a composition that reads on the specific components recited in claim 63, assuming water would be required in that claim.

7. Applicant's arguments, see pp. 17-18, with respect to the rejection of claims 19-30 as being unpatentable over Yakuji Nippo Ltd. and Xia; and claims 19-38 as being unpatentable over Yakuji Nippo Ltd., Xia, and Nolan have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as follows.

8. Claims 19-38, 41-60 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 41-60 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is necessitated by the amendment introducing new claims.

11. With respect to claims 41-60, the recitation of the transitional phrase generally considered to refer to closed claim language, "consisting essentially of" together with the open language term, "at least" in the 1st line of claim 41, is not clear whether open construction or closed construction is meant by the claim; additionally the language of

the 1st and 2nd components, “comprising”, an open construction term is also unclear and inconsistent with the closed construction phrase, “consisting essentially of”. It is not clear whether formulations containing the recited components and additional components would fall within or outside of the metes and bounds of the instant claims. For other rejections the phrase "consisting essentially of at least" is construed to have the same meaning as "comprising", consistent with the broadest reasonable interpretation of these claims.

12. With respect to claim 63, the recitation of the transitional phrase, “consisting of" the two components, each of which use the term, “comprising” to recite the compounds present in each components, does not make clear whether the claim construction is closed or open; i.e., it is not clear whether a formulation containing one compound from the 1st component, one compound from the 2nd component, one or more of the optional components recited and at least one non-component compound (not recited in the claim), such as water or an alcohol, would fall within the scope of or be excluded from the subject matter of the claim. For prior art rejections, the claims are construed in the broader meaning, i.e., the presence of "comprising” in the claim has the meaning of open ended claim construction.

13. Additionally, claim 63 recites “an aqueous liquid preparation” consisting of two required components, and optionally containing at least one additional component, none of the required or optional components recite water. The presence of an “aqueous” preparation along with the absence of water is inconsistent, and does not make clear whether water is required, optional or absent.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

14. Claims 19-38, 41-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellberg et al. (US 5,998,465; 1999) and Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; cited with previous Interview Summary).

15. Hellberg teaches pharmaceutical compositions of anti-inflammatory compounds (abstract); the compounds include a non-steroidal anti-inflammatory moiety (NSAIA) and an antioxidant moiety linked through an ester bond formed by the carboxylic acid moiety of the NSAIA (col. 2, lines 20-24); NSAIA moieties include bromfenac (col. 3, line 57; claim 5); examples 2 and 3 (col. 11) teach topical ophthalmic formulations useful for treating inflammation, both of these formulations include tyloxapol at 0.01-0.05 w/v %, HPMC (thickener), benzalkonium chloride (preservative), edetate disodium (chelating agent) (col. 11, Examples 2-3); the pH is adjusted to 7.4 (about 7.5; col. 11, line 64); topical formulations administered by drops (eyedrops; col. 10, lines 15-18). Hellberg does not teach bromfenac (only the ester of bromfenac). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute bromfenac, taught by Nolan for the compounds of Hellberg in the example formulation giving formulations of the instant claims and to select concentrations of

bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would also have been obvious to adjust the concentration of tyloxapol, to optimize the formulations for the effect would on the solubility and stability of the aqueous preparations, which would have resulted in the effective tyloxapol concentrations of about 0.02 and 0.3 w/v%, recited in claims 25 and 32. The motivation to substitute bromfenac in the Hellberg formulations would have bee the art-recognized equivalent activity of bromfenac as an anti-inflammatory agent in topical usage. The motivation to adjust concentrations would have been the routine optimization of these topical ophthalmic formulations for anti-inflammatory use in the eye.

Double Patenting

16. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

17. Claims 41-60 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 19-38. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

This objection is necessitated by the amendment adding new claims. Claim 41 uses the transitional phrase in the preamble, "consisting essentially of at least", whereas claim 19 uses the transitional phrase, "comprising"; all other wording is identical. "Consisting essentially of" is generally closed language, excluding components not recited in the claim. However, the presence of the open language term, "at least" removes the closed language of "consisting essentially of", giving the meaning that the recited components are required, but additional components no recited may optionally be present, which is the same meaning possessed by the term, "comprising". Therefore, though the two sets of claims use slightly different wording, the meanings are the same.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614